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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,710	02/24/2004	Mark L. Nelson	PAZ-025CPCN	3651
959	7590	01/05/2006	EXAMINER	
LAHIVE & COCKFIELD, LLP. 28 STATE STREET BOSTON, MA 02109			FREISTEIN, ANDREW B	
			ART UNIT	PAPER NUMBER
			1626	
DATE MAILED: 01/05/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/786,710

Applicant(s)

NELSON ET AL.

Examiner

Andrew B. Freistein

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-76 & 82 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13, 16, 18-22, 27, 28, 41-55, 63, 69-76 and 82 is/are rejected.
- 7) ☒ Claim(s) 14, 15, 17, 23-26, 29-40, 56-62 and 64-68 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/22/2005</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-82 are currently pending. Claims 83-102 were cancelled.

Priority

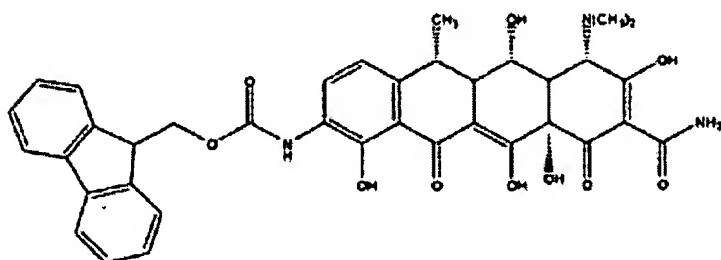
This application is a Continuation of US Application No. 09/823,884, filed 03/30/2001, which granted as US Pat. No., which claims benefit of US Provisional Application No. 60/193,879, filed 03/31/2000, US Provisional Application No. 60/193,972, filed 03/31/2000, and US Provisional Application No. 60/280,367, filed 03/29/2001.

Information Disclosure Statement

Applicant's information disclosure statement (IDS), filed on 02/22/2005, has been considered. Please refer to Applicant's copies of the 1449 submitted herewith.

Response to Restriction Requirement

Acknowledgement is made of Applicant's election (without traverse) of Group I
and, for search purposes, the species,



, in a response filed 11/09/2005.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1626

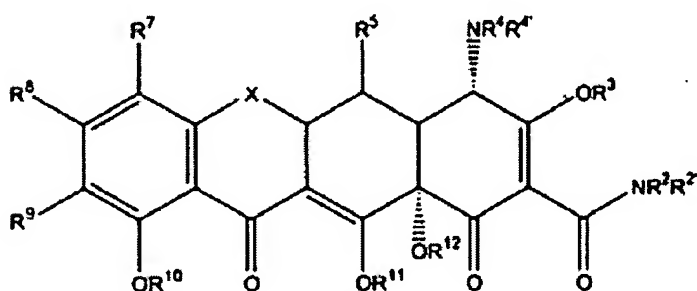
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 11-13, 16, 18-20, 22 and 82 are rejected under 35 U.S.C. 102(b)

as being anticipated by Barden et al, "Glycylcyclines' 3. 9-

Aminodoxycyclinecarboxamides," J. Med. Chem., 37(20), 3205-11 (1994).

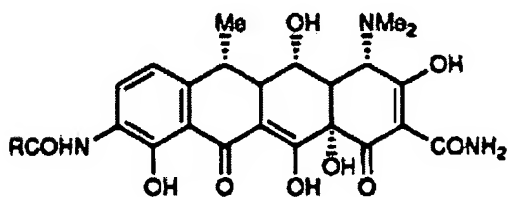
The instant application claims a compound of formula (I),



, wherein X is CR'R⁶; R², R^{2'}, R³,

R⁶, R⁷, R⁸, R^{9c}, R¹⁰, R¹¹ and R¹² are H; R⁴, R^{4'}, R^{6'}, and R^{9a} are alkyl; R⁵ is hydroxyl; R⁹ is NR^{9c}C(=Z')ZR^{9a}; Z is CR^dR^e, N^{Rb}, or O; Z' is O; and R^b, R^d and R^e are independently H or alkyl.

Barden et al. disclose the compound and pharmaceutical composition comprising the compound comprising the compound of the formula



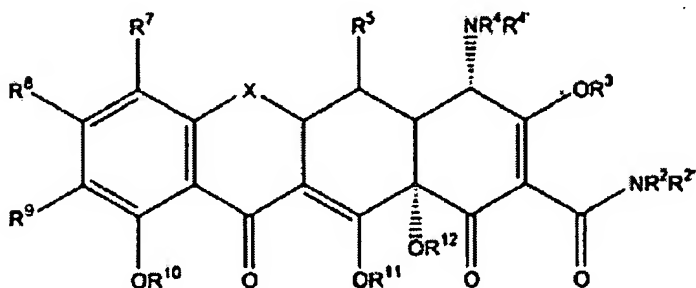
, wherein R is Me₂CH, MeO, (CH₂)₄NCH₂,

(CH₂)₅NCH₂, Me₂NCH₂, Et₂NCH₂, *t*-C₄H₉NHCH₂, *n*-C₄H₉NHCH₂ (see p. 3206, col. 1, scheme 2a).

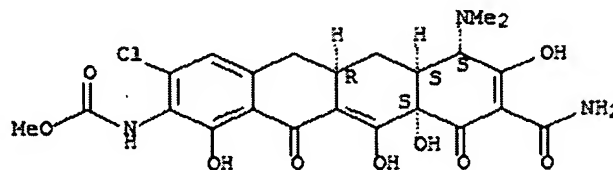
Art Unit: 1626

Claims 1, 11-13, 16, 19, 20-22 and 82 are rejected under 35 U.S.C. 102(b) as being anticipated by Sum et al., US Pat. No. 5,430,162.

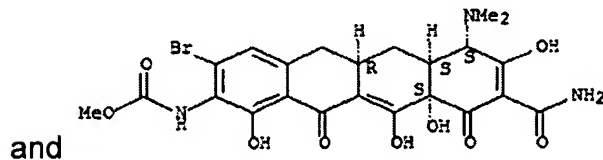
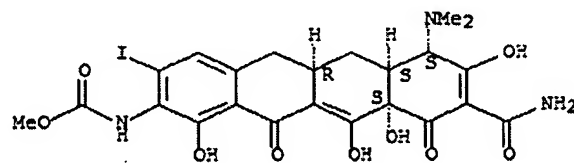
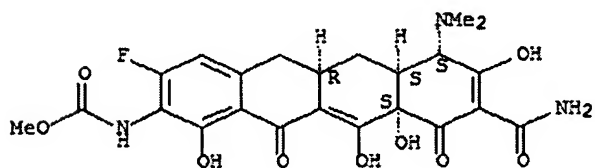
The instant application claims a compound of formula (I),



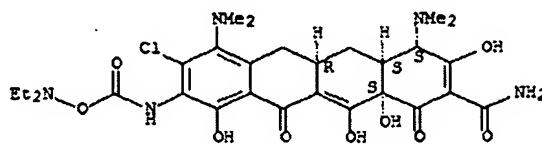
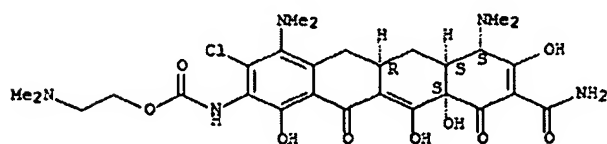
, wherein X is CR^6R^6 ; R^6 , R^2 , R^2 , R^3 , R^6 , R^7 , R^{9c} , R^{10} , R^{11} and R^{12} are H; R^4 , R^4 , and R^{9a} are alkyl; R^5 is hydroxyl; R^9 is $NR^{9c}C(=Z')ZR^{9a}$; Z is O; Z' is O; and R^8 is halogen.



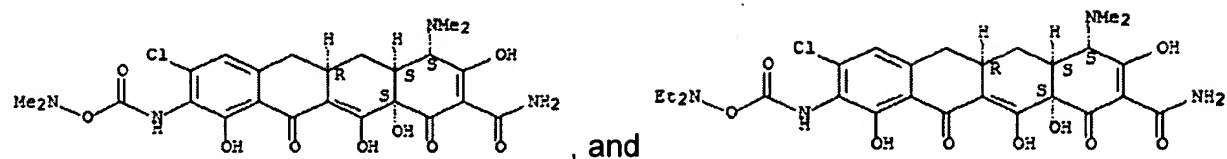
Sum et al. disclose the compounds:



and



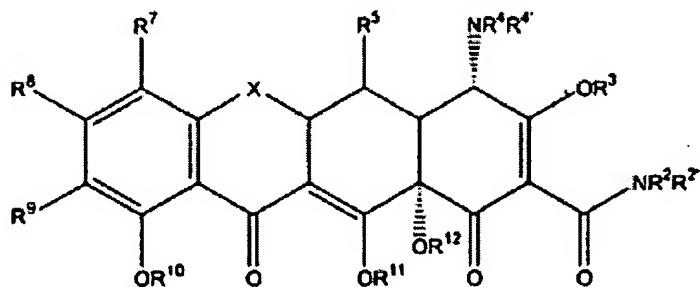
Art Unit: 1626



and pharmaceutical compositions comprising the compounds (see Sum et al., STN International (2005), HCAPLUS Database, Accession No. 1994:579403, Reg. Nos. 157579-07-2, 157579-18-5, 157579-36-7, 157579-37-8, 157579-23-2, 157579-22-1, 157579-30-1, and 157579-31-2).

Claims 1-6, 11-13, 16, 20-22 and 82 are rejected under 35 U.S.C. 102(b) as being anticipated by Hlauka et al., US Pat. No. 5,494,903.

The instant application claims a compound of formula (I),

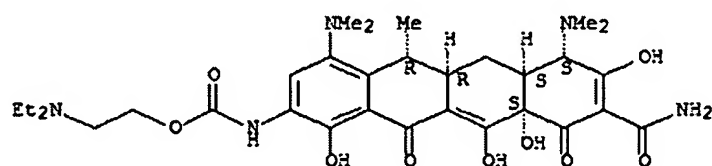


, wherein X is CR'R⁶; R², R^{2'}, R³,

R⁶, R⁸, R^{9c}, R¹⁰, R¹¹ and R¹² are each H; R⁴, R^{4'}, and R^{6'} are alkyl; R⁹ is

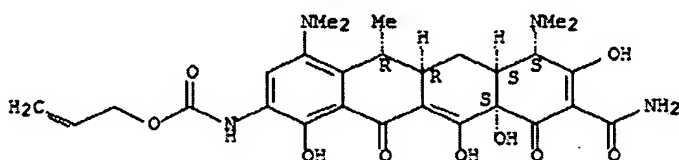
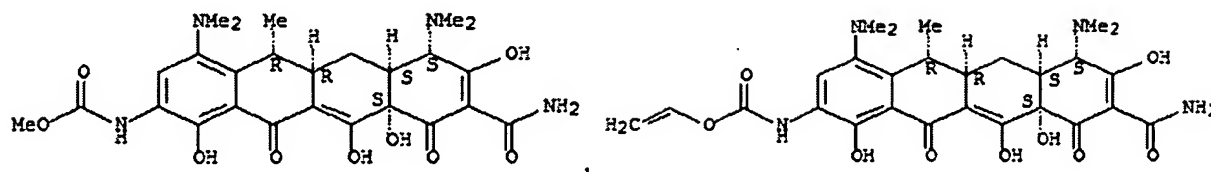
NR^{9c}C(=Z')ZR^{9a}; Z is O; Z' is O; and R^{9a} is alkyl or alkenyl.

Hlauka et al. disclose the compounds and pharmaceutical compositions



comprising the compounds:

Art Unit: 1626



and

(see Hlauka et al., STN

International (2005), HCAPLUS Database, Accession No. 1993:603237, Reg. Nos. 150251-75-5, 150231-23-5, 150251-75-5, and 150251-77-7).

Claim Rejections – Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

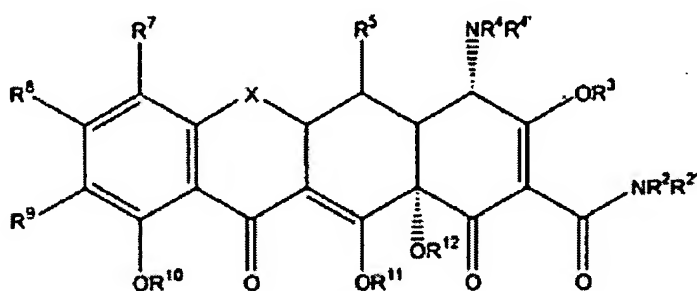
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the confliction application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Art Unit: 1626

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10, 41-55, 69-76, and 82 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-26, 32 and 51-81 of U.S. Pat. No. 6,818,634 (the '634 patent).

The instant application claims a compound and pharmaceutical composition comprising a compound of formula (I),



, wherein:

Art Unit: 1626

X is $\text{CHC}(\text{R}^{13}\text{Y}'\text{Y})$, CR^6R^6 , S, NR^6 , or O;

R^2 is hydrogen, alkyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^4 and $\text{R}^{4'}$ are each hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^2 , R^3 , R^{10} , R^{11} and R^{12} are each hydrogen or a pro-drug moiety;

R^5 is hydrogen, hydroxyl, or a prodrug moiety;

R^6 , $\text{R}^{6'}$, and R^8 are each independently hydrogen, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, or halogen;

R^7 is hydrogen, dialkylamino, heteroaryl-amino, or $\text{NR}^{7c}\text{C}(=\text{W}')\text{WR}^{7a}$;

R^{13} is hydrogen, hydroxy, alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an arylalkyl;

Y' and Y are each independently hydrogen; halogen; hydroxyl; cyano, sulfhydryl; amino; alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an arylalkyl;

R^9 is hydrogen, $\text{NR}^{9c}\text{C}(=\text{Z}')\text{ZR}^{9a}$, or heteroaryl-amino;

Z is $\text{CR}^{9d}\text{R}^{9c}$, NR^{9b} , or O;

Z' is O or S;

R^{9a} , R^{9b} , R^{9c} , R^{9d} , and R^{9e} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylsulfonyl, alkoxycarbonyl,

arylcarbonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic, absent, or a prodrug moiety, and R^{9d} and R^{9e} may be linked to form a ring;

W is $\text{CR}^{7d}\text{R}^{7c}$, NR^{7b} or O;

W' is O or S; and

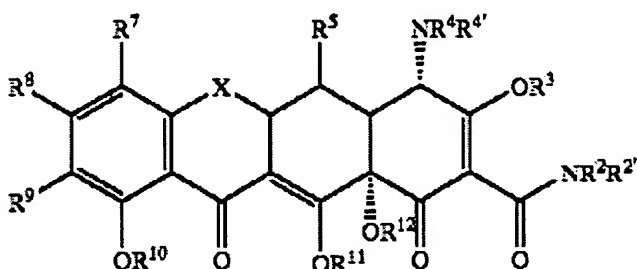
R^{7a} , R^{7b} , R^{7c} , R^{7d} , and R^{7e} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, arylsulfonyl, alkoxycarbonyl, arylcarbonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic, absent, or a prodrug moiety, and R^{7d} and R^{7e} may be linked to form a ring;

and pharmaceutically acceptable salts thereof, provided that at least one of R^9 is not hydrogen when R^7 is hydrogen or dialkylamino.

Art Unit: 1626

Determining the Scope and Content of the Prior Art

The '634 patent claims a compound and pharmaceutical composition comprising



the compound of formula (I),

, wherein

X is $\text{CHC}(\text{R}^{13}\text{Y}^*\text{Y})$, CR^6R^6 , S, NR^6 , or O;

R^2 is hydrogen, alkyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^4 and $\text{R}^{4'}$ are each hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$\text{R}^{2'}$, R^3 , R^{10} , R^{11} and R^{12} are each hydrogen or a pro-drug moiety;

R^5 is hydrogen, hydroxyl, or a prodrug moiety;

R^6 , $\text{R}^{6'}$, and R^8 are each independently hydrogen, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, or halogen;

R^7 is hydrogen, dialkylamino, or heteroaryl-amino;

R^{13} is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino; or an arylalkyl;

Y^* and Y are each independently hydrogen; halogen; hydroxyl; cyano, sulfhydryl; amino; alkyl; alkenyl; alkynyl; alkoxy; alkylthio; alkylsulfinyl; alkylsulfonyl; alkylamino; or an arylalkyl;

R^9 is hydrogen, or heteroaryl-amino;

and pharmaceutically acceptable salts thereof, provided that R^9 is not hydrogen when R^7 is hydrogen or dialkylamino.

Ascertaining the Differences Between the Instant Application and the Prior Art

Art Unit: 1626

The instant application claims R^7 to be H, dialkylamino, or $NR^{7c}C(=W')WR^{7a}$; and claims R^9 to be H, $NR^{9c}C(=Z')ZR^{9a}$, or heteroaryl-amino. The '634 patent does not claim R^7 to be $NR^{7c}C(=W')WR^{7a}$ and does not claim R^9 to be $NR^{9c}C(=Z')ZR^{9a}$.

Finding Prima Facie Obviousness

The products claimed in the instant application are disclosed in the prior art. Particular species are claimed in the prior art and in the instant application. For example, claim 23 of the '643 patent claims the exact same species as claimed in claim 53 of the instant application. One of ordinary skill in the art would be motivated to produce the compounds of the instant application with the disclosure of the '643 patent. Moreover, there is nothing the prosecution history of the '643 to indicate why the Applicant could not have pursued the instant claims in the prior patent application. Therefore, claims **1-10, 41-55, 69-76, and 82** are rejected under the judicially created doctrine of obviousness-type double patenting.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5, 9, 19, 27-28, 63 and 82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(1) Claims **1, 9, and 82** define variables R^2 , R^4 , $R^{4'}$, R^5 , R^{9a-e} , and R^{7a-e} use the term "prodrug moiety" to define the variables. "Prodrug moiety" is defined to be "moieties which can be metabolized in vivo to yield an active compound" and provides

Art Unit: 1626

examples (see Spec., p. 24, lines 18+). Exemplification is not an explicit definition. The specification must set forth the definition explicitly and clearly, with reasonable clarity, deliberateness and precision. *Teleflex Inc. v. Ficosa North Am Corp.*, 63 USPQ2d 1374, (Fed. Cir. 2002), *Rexnord Corp. v. Laitram Corp.*, 60 USPQ2d 1854 (Fed. Cir. 2001).

Claims 1, 9 and 82 should delete “prodrug moiety” in every instance in the claims.

(2) Claim 5 states a compound of claim 4 wherein said compound is a *derivative* of tetracycline, minocycline, sancycline... (emphasis added). A derivative is something copied or obtained from something else. Thus, claiming a derivative of another product is the equivalent of claiming the process of producing it. However, claim 5 is a product claim and not a process claim, because there are no steps to show a process of producing the product. Claim 5 must specifically define the product it claims rather than a product of a process.

(3) Claims 19 and 27 claim a compound wherein R^{9a} is multicyclic and claim 63 claims a compound wherein R^{7a} is multicyclic. The specification defines “multicycle,” but does not define “multicyclic.” Rather, the specification defines examples of “multicyclic moieties” (see p. 23, lines 24-34). Exemplification is not an explicit definition. The specification must set forth the definition explicitly and clearly, with reasonable clarity, deliberateness and precision. *Teleflex Inc. v. Ficosa North Am Corp.*, 63 USPQ2d 1374, (Fed. Cir. 2002), *Rexnord Corp. v. Laitram Corp.*, 60 USPQ2d 1854 (Fed. Cir. 2001). Claims 19 and 27 must be amended to specifically identify the multicyclic moieties that are to be alternatives in the Markush-type claim.

Art Unit: 1626

(4) Claims 28 claims a compound of formula (I), wherein R^{9a} is "steroidyl."

There is no definition of "steroidyl" in the specification. A "steroid" is any of number of naturally occurring or synthetic fat-soluble organic compounds having as a basis 17 carbon atoms arranged in four rings and including the sterols and bile acids, adrenal and sex hormones, certain natural drugs such as digitalis compounds, and the precursors of certain vitamins. The specification must set forth the definition explicitly and clearly, with reasonable clarity, deliberateness and precision. *Teleflex Inc. v. Ficosa North Am Corp.*, 63 USPQ2d 1374, (Fed. Cir. 2002); *Rexnord Corp. v. Laitram Corp.*, 60 USPQ2d 1854 (Fed. Cir. 2001).

Claim Objections

Claims 53 and 55 are objected to because of the following informalities:

(1) Claims 53 and 55 each claim a long list of compounds. Before the second to last compound in each claim there should be an "and" inserted in the claims.

(2) Claim 55 should end with a period.

Appropriate correction is required.

Claims 14-18, 20-26, 29-40, 56-62 and 64-68 are objected to as being dependent upon a rejected base claim. However, these claims would be deemed allowable if written in independent form or appropriate correction is made on the claims upon which they depend.


Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached Monday-Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^cKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Andrew B. Freistein
Patent Examiner, AU 1626



Taofiq Solola, J.D., Ph.D.
Primary Patent Examiner, AU 1626
Date: December 28, 2005